adrenals. Autoradiography of skin fibroblast culture demonstrated that the cell line with 48 chromosome included a distinctly late-labelled X chromosome and an extra D chromosome labelling as expected for No. 13. The labelling in the 47 chromosome cell line also confirmed the extra D to be No. 13. No euploid cells were found. Chromosome analysis of peripheral blood from each parent was normal.

Discussion

Pergament and Kadotani (1965) found trisomy D and XXY in a tissue culture from the limb-bud of an early spontaneous abortion. Although our patient is the first reported liveborn infant with trisomy 13 and an XXY sex chromosome complement, we are aware of another such infant through a personal communication (C. B. Francisco and C. Herzon). That infant lived 2 hours and also had physical features consistent with trisomy D_1 syndrome. It is noteworthy that the double aneuploidy in our patient would have been undetected if only peripheral blood had been examined.

There are at least 4 possibilities for the mechanism by which an individual can be mosaic for single and double aneuploidy. The first is fertilization between a normal gamete and a gamete with an extra chromosome resulting in a trisomic zygote; ie, 47,XY,13+, followed by a subsequent non-disjunction producing a double aneuploid line (48, XXY,13+). The other cell line of 46,Y,13+ is presumably non-viable. A second possibility entails an initially euploid zygote followed by 2 non-disjunctional events resulting in 46,XY/47,XY,13+/48,XXY,13+ cell lines. This explanation is less satisfactory since a normal euploid cell line was not found in our patient. A third possibility is the fertilization of 2 gametes each with an extra chromosome, resulting in a doubly aneuploid zygote; namely, 48,XXY,13+. A later non-disjunction could then result in one cell line trisomic for only the No. 13 chromosome and another cell line of 49,XXXY,13+, presumably non-viable. A fourth possibility is that of anaphase lag occurring in a double aneuploid 48,XXY,13+ zygote, producing 48,XXY,13+/47,XY,13+ mosaicism. However, the fact that 48,XXY,13+ is the minor cell line is against it. The simplest explanation involving the fewest number of division errors is the first possibility.

REFERENCE

Pergament, E. and Kadotani, T. (1965). A new double aneuploid: XXY D trisomy. *Lancet*, **2**, 695.

ALLAN J. EBBIN, ROSIE CHU LIM,
JOSEPH W. TOWNER, and MIRIAM G. WILSON

*Department of Pediatrics, Los Angeles County–
University of Southern California Medical Center
and University of Southern California School of
Medicine, Los Angeles, California, USA*

A Case of Partial 14 Trisomy 47,XY,(14q−)+ and Translocation t(9p+;14q−) in Mother and Brother*

D group trisomy (13–15) was first described by Patau *et al* in 1960. Since then at least 126 cases with cytological confirmation have been reported (Taylor *et al*, 1970). The phenotypic features have been tabulated and considerable variations noted. In some of these cases the extra chromosome was identified by autoradiographic techniques (Giannelli, 1965) and recently in 2 cases by quinacrine fluorescence (D. A. Miller *et al*, 1971) as a No. 13. The rest have been presumed to be 13 trisomy because of the clinical similarity of the phenotype. A syndrome associated with trisomy of chromosome 14 has not been described. We report here a case trisomic for a large part of chromosome 14 identified by quinacrine fluorescence.

Family studies revealed a translocation, t(9p+; 14q−), involving the long arm of chromosome 14 and the short arm of chromosome 9 in the mother and an older sib of the propositus, both phenotypically normal. The case represents transmission, presumably by non-disjunction, of the structurally abnormal chromosome 14 (14q−) from the translocation carrier mother producing a child partially trisomic for 14 [47,XY,(14q−)+].

Family History

The pedigree is detailed in Fig. 1. The propositus (III.3) was the product of the 3rd pregnancy of a

phenotypically normal mother (II.5) aged 22 at the time of his birth. The father (II.4) was aged 27 and also phenotypically normal. There is no history of consanguinity. The first pregnancy resulted in a spontaneous abortion at 2 months gestation (III.1). The second pregnancy resulted in a phenotypically normal male child (III.2). There is no family history of consanguinity, mental retardation, or congenital malformations. A female sib (II.6) of the mother died in the neonatal period, reportedly of hyaline membrane disease, but she is not known to have had any congenital malformations.
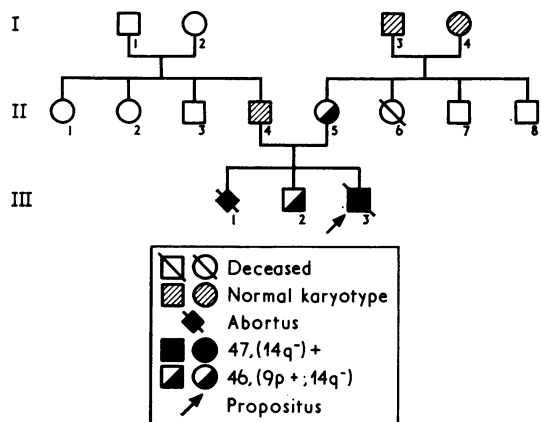
Case Report

The propositus (III.3; BB-111270*) was the product of a normal pregnancy and delivery. Physical examination revealed a small, tachypnoeic male infant with perioral cyanosis. Birth weight was 2910 g (40th centile), head circumference 32 cm (below 3rd centile), and length 42 cm (below 3rd centile). The microcephalic head was characterized by a small fontanelle and sloping forehead (see Fig. 2). There was microphthalmia with hypotelorism. The ears were low-set and posteriorly rotated with malformed pinnae. There was nasal beaking and a hypoplastic mandible. The maxillary alveolar ridge was centrally cleft but the palate was intact and normal. He had a short neck, barrel chest, and

* Case identification as suggested by the Chicago Conference (1966). Initials (BB) followed by date of birth—day (11), month (12), and year (70). This patient is also so cited by D. A. Miller *et al* (1971).
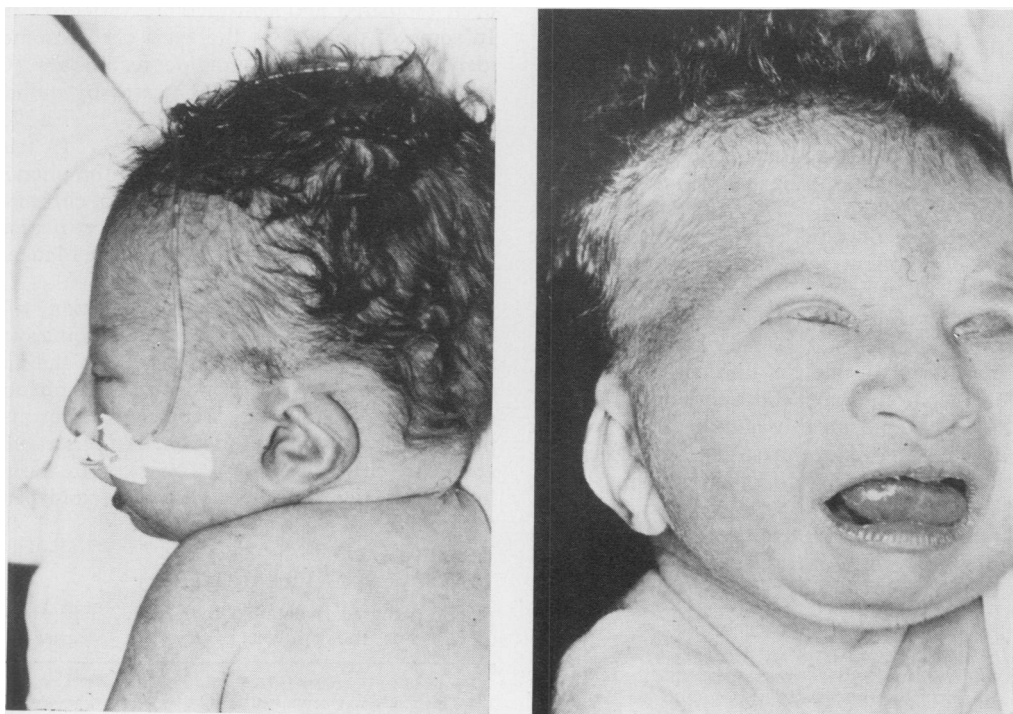

Legend:
☒ ⊘ Deceased
▨ ⊘ Normal karyotype
◆ Abortus
■ ● 47,(14q⁻)+
◪ ◑ 46,(9p+;14q⁻)
↗ Propositus

FIG. 1. Pedigree of the family.

FIG. 2. Head and face of propositus.

kyphotic spine. The heart rate was 154 and a soft, early systolic murmur was heard at the 4th LICS with a single second heart sound. Although there was marked tachypnoea, breath sounds were normal and there were no retractions. The liver edge was palpable 2 cm below the right costal margin. The penis was quite small. A normal right testis was palpable, and no left testis could be felt. There were bilateral simian creases and finger contractures, as well as equinovarus deformity of the right foot and valgus deformity of the left foot. There was intermittent extensor rigidity. Motor tone and Moro reflex were poor, but a strong suck reflex was present. His cry was high-pitched.

Radiology revealed cardiomegaly with increased lung markings. In addition, there was an unusual configuration of the upper thoracic spine and ribs causing the ribs to be orientated horizontally rather than inclined downward.

Over the 60 hours from admission to death the infant developed progressive congestive heart failure with increasing cardiomegaly, hepatomegaly, tachypnoea, and cyanosis. Generalized seizure activity and extensor posturing were repeatedly observed. Intolerance to oral feedings with vomiting, delayed gastric emptying, and diarrhoea developed. Death from progressive cardiopulmonary failure occurred 72 hours after birth.

Pathology. At necropsy the body weight was 2780 g. Pertinent measurements included crown-rump length—30 cm; crown-heel length—43 cm; head circumference—32 cm; and chest circumference—31 cm.

Gross examination of the heart disclosed a secundum septal defect with marked attenuation of the atrial flap. The gallbladder and its associated duct were absent; however, the other portions of the extrahepatic biliary tree appeared normal. No other gross abnormalities were discernible, although the thymus was small, weighing only 2·5 g. The brain weight was 350 g and there were no obvious external abnormalities. The major convolutions were well-formed and the gyral pattern appeared to be that of a full-term infant. Microscopic examination revealed an immature cortical cytoarchitecture in the cerebrum and cerebellum with marked vascular congestion and extensive autolytic change. Myelin stains demonstrated pallor of the white matter throughout, but there was no evidence of myelin breakdown.

Cytogenetic Studies

Methods. Chromosome studies were done on cultured phytohaemagglutin-stimulated leucocytes. Slides with spread metaphase figures from cultured leucocytes were stained, with either orcein or
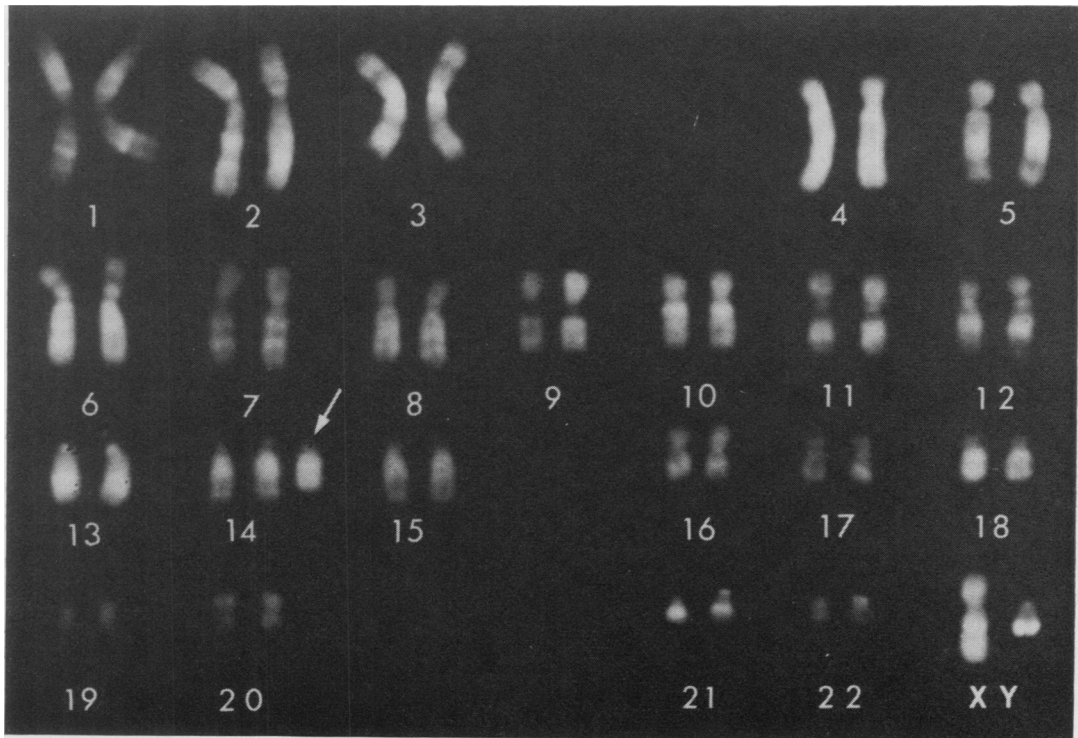

FIG. 3. Karyotype of the propositus. All the numbered pairs show the quinacrine fluorescent patterns of normal chromosomes. The arrow designates the extra No. 14 with partial deletion of the long arm.
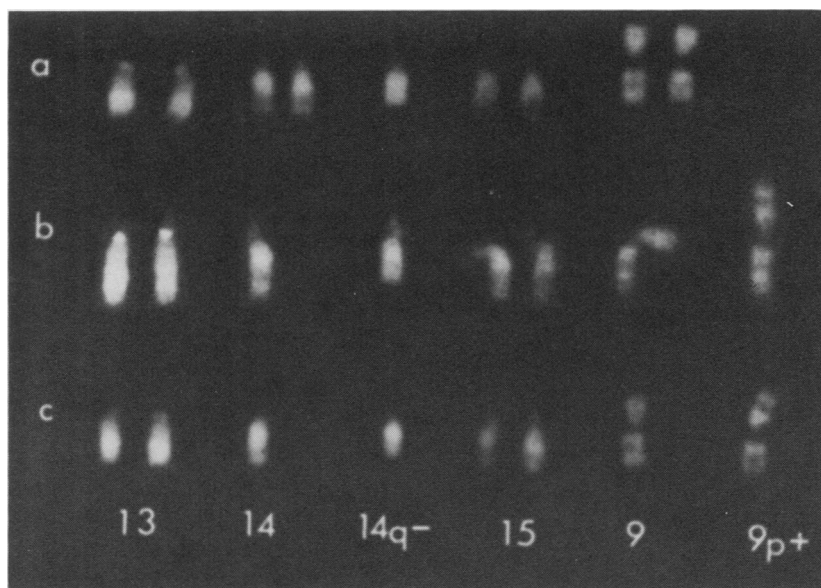
Case Reports

FIG. 4. Partial karyotypes of cells from propositus (a), mother (b), and sib (c). Numbers designate the chromosomes.

quinacrine. Our method for examining chromosomes by quinacrine fluorescence is as follows (Breg, 1972): slides were stained for 5 min in a 0·5% aqueous quinacrine dihydrochloride solution (Atebrin, G. Gurr), rinsed in running tap water for 3 min, then rinsed and mounted in Tris-maleate buffer at pH 5·6. Cells were then examined with a Leitz microscope equipped with a mercury vapour lamp, a 3 mm BG 12 exciter filter, darkfield condenser, and K510 barrier filter. Photographs of suitable metaphase cells were made with a Leitz Kavar attachment camera and an 8 × eyepiece on either 35 mm Kodak Panatonic-X or H & W Control VTE Panchromatic film. Karyotypes were then prepared following the arrangement published by Caspersson, Lomakka, and Zech (1971).

Findings. On study of both orcein- and quinacrine-stained cells from the patient, an extra D-group chromosome, the long arm of which appeared unusually short, was found (Figs. 3 and 4a). Since this chromosome had a portion missing and did not replace any normal chromosome, its identification, even by its fluorescence pattern, was uncertain. However, the identity of this chromosome became apparent when it was again found in the mother's cells. The mother's cells contained 46 chromosomes and her karyotype included 2 abnormal chromosomes. The short arm of a chromosome

9 was lengthened while the distal end of the long arm of a No. 14 was comparably deleted (Fig. 4b). Thus the mother was the carrier of a reciprocal translocation, t(9p + ;14q −). The same translocation was found in the mother's only living offspring (III.2) (Fig. 4c). The translocation in both of these normal individuals is presumed to be balanced although a portion of No. 9 could not be identified on chromosome 14. The patient therefore is trisomic for approximately three-fourths of chromosome 14 [47,XY,(14q −) +]. The chromosomes of the father (II.4) and both maternal grandparents (I.3 and I.4) were normal.

Blood Group Studies

Table I shows the results of the gene marker studies done on members of this pedigree. No anomalous inheritance of any of the markers studied was found.

Discussion

Cytogenetic Findings. Every normal human metaphase chromosome can be identified by its characteristic quinacrine fluorescence banding pattern. This method is superior to either orcein morphology or terminal DNA replication, methods by which only some of the chromosomes can be specifically identified. Since many chromosomes also have specific regional patterns it is now possible

TABLE I
RESULTS OF GENE MARKER STUDIES

Family Member	ABO	Rh	P	K	k	Kp	MNS	Lu^a	Fy^a	Jk^a	Xq^a
I.3	O	CDEce	+	−	+	b+	MNs	−	−	+	+
I.4	A	CDe	+	−	+	b+	MNs	−	+	+	+
II.4	A$_1$	CEc	+	−	+	b+	Ms	−	+	+	+
II.5	A	DCe	+	−	+	b+	MNs	−	−	+	+
III.2	A$_1$	DCEce	+	−	+	b+	Ms	−	−	+	+

to identify abnormalities which were previously undetectable. In particular, in translocations the patterns of the exchanged regions of chromosomes do not appear to be altered, making possible the identification of the involved chromosomes and the break points (Breg *et al*, 1972).

This technique made possible identification of the specific chromosomal abnormalities in this patient, his mother and brother. The propositus' mother (II.5) was identified as a phenotypically normal carrier of a reciprocal translocation involving chromosomes 9 and 14. While in our case a large piece of No. 14 is located on the short arm of No. 9, it has not been possible to identify the small portion of No. 9 presumed to be on chromosome 14.

During meiosis in a translocation carrier some of the gametes formed may contain duplications, deficiencies, or both (Ford and Clegg, 1969). Meiotic segregation by alternate or adjacent migration of centromeres (see Fig. 5) in this mother would produce 6 types of gametes, one normal, one translocation carrier like herself, and 4 duplication or deficiency gametes. Such segregation would account for the presence in this pedigree of the translocation carrier offspring (III.2).

None of the segregational events described above accounts for the karyotype of the propositus (III.3) which has an extra chromosome and must be the result of a non-disjunction of the mother's chromosomes 14 during meiosis. Eight different abnormal gametes could be produced by disjunctional errors involving the 2 translocational chromosomes in this mother. The distribution of chromosomes 9 and 14 at disjunction which would result in the karyotype of our patient is depicted in Fig. 5. Several reports (Jacobsen, Dupont, and Mikkelsen, 1963; Hauschteck *et al*, 1966; Brøgger, 1967; J. R. Miller *et al*, 1970) suggest that the presence of a translocation may predispose to mis-segregation at meiosis, even among chromosomes not directly involved in the translocation.

Clinical Findings. Table II compares the physical features of this patient with those found in at least 50% of Patau's syndrome cases as reviewed by Taylor (1968). These are presumed to be cases of 13 trisomy on the basis of conventional stain techniques. D. A. Miller *et al* (1971), have recently reported quinacrine fluorescence identification of an extra 13 chromosome in 2 cases with these

	Chromosomes				Gametes	Karyotype of zygote
	14	14q⁻	9	9p⁺		
Alternate segregation to yield sibling (III-2)					14, 9	Normal
					14q⁻, 9p⁺	Balanced translocation carrier- [SIBLING]
Adjacent 1 segregation					14q⁻, 9	14 deletion Phenotype unknown
					14, 9p⁺	14 duplication Phenotype unknown
Adjacent 2 segregation					9, 9p⁺	Monosomy 14, Trisomy 9 Presumed lethal
					14, 14q⁻	Monosomy 9, Trisomy 14 Presumed lethal
Nondisjunction to yield proband (III-3)					9p⁺	Monosomy 14 Presumed lethal
					14, 14q⁻, 9	Trisomy for ¾ of No 14 [PROBAND]

FIG. 5. Segregation and non-disjunction in a translocation carrier at meiosis.

TABLE II
CLINICAL FEATURES OF 13 TRISOMY AND 14 TRISOMY

Clinical Features	D₁ Trisomy (>50% of cases)	14 Trisomy (Murken et al, 1970)	14 Trisomy (Allerdice et al, 1972)	14 Trisomy (present case)
Failure to thrive	+	+	+	+
Death in early infancy	+	O	O	+
Microcephaly	+	O	+	+
Mental retardation	+	+	+	N
Seizures	O	O	+	+
Apnoeic spells	+	O	O	+
Arrhinencephaly	+	N	N	O
Microphthalmia	+	O	+	+
Eye defect	+	O	O	O
Hypertelorism	+	+	O	O
Flat nasal bridge	O	+	O	+
Low set ears	+	+	+	+
Anomalous pinnae	+	+	O	+
Apparent deafness	+	O	O	N
Cleft lip and palate	+	O	O	O
High arched palate	O	O	+	O
Micrognathia	+	+	+	+
Capillary haemangiomata	+	O	O	O
Septal cardiac defect or PDA	+	O	O	+
Polydactyly	+	O	O	O
Simian creases	+	O	O	+
Flexion contractures-fingers	+	O	O	+
Overlapping finger postures	O	O	O	+
Hyperconvex, long fingernails	+	+	O	O
Talipes equinovarus	O	O	O	+
Undescended testes	+	N	N	+
Biseptate uterus	+	N	N	N

+ = present; O = absent; N = not observed or not applicable.

phenotypic features, and it is probable that most of the other patients with the clinical diagnosis of D trisomy were trisomic for No. 13.

It is not yet possible to delineate a syndrome associated with 14 trisomy. There are no reported individuals who undoubtedly are trisomic for all of No. 14. Murken *et al* (1970), reported a case with 7 D-group chromosomes, 3 of which had the DNA replication pattern compatible with No. 14. However, this cannot be considered conclusive identification of the extra chromosome. In a similar case studied by Allerdice *et al* (1971), an extra D-group chromosome had a DNA replication pattern of No. 14, but on later study by quinacrine fluorescence this chromosome proved to be the proximal third of a No. 14 and the translocated long arm of a No. 6. The patient was therefore trisomic for about a third of the proximal portion of chromosome 14. The features of these 2 cases are also listed in Table II for comparison.

The features thus far compiled suggest that within D-group trisomies, cleft lip and palate, capillary haemangiomata, deafness, arrhinencephaly, and polydactyly are limited to 13 trisomy. Such non-specific features as abnormal ears, cardiac defects, seizures and mental retardation, simian creases, genital abnormalities, and failure to thrive are common to 13 and 14 trisomy, as they are to certain other autosomal trisomies.

Summary

The clinical features and quinacrine fluorescent cytogenetic studies of a case of partial 14 trisomy [47,XY,(14q −)+] are presented. Precise identification of the extra chromosome was made possible by study of the karyotype of the mother which showed a reciprocal translocation involving chromosomes 9 and 14. This translocation [t(9p + ; 14q −)] was also present in the propositus' sib but not in the mother's parents.

ELIZABETH M. SHORT
Division of Medical Genetics, Departments of Medicine and Pediatrics, Yale University School of Medicine, New Haven, Connecticut, USA

GILBERT B. SOLITARE
Department of Pathology, Yale University School of Medicine, USA

W. ROY BREG
Department of Pediatrics, Yale University School of Medicine and Southbury Training School, Southbury, Connecticut, USA

REFERENCES

Allerdice, P., Miller, O. J., Miller, D. A., Breg, W. R., Gendel, E., and Zelson, C. (1971). Familial translocation involving chromosomes 6, 14, and 20 identified by quinacrine fluorescence. *Humangenetik*, **13**, 205–209.

Breg, W. R. (1972). Quinacrine fluorescence for identifying metaphase chromosomes, with special reference to photomicrography. *Stain Technology*, **47**, 87–93.

Breg, W. R., Miller, O. J., Miller, D. A., and Allerdice, P. W. (1972). Identifications of reciprocal translocation chromosomes by quinacrine fluorescence. *American Journal of Diseases of Children*, **123**, 561–564.

Brøgger, A. (1967). *Translocations in Human Chromosomes*, p. 110. Universitets Forlaget, Oslo.

Caspersson, T., Lomakka, G., and Zech, L. (1971). The 24 fluorescence patterns of the human metaphase chromosomes-distinguishing characters and variability. *Hereditas, Genetiskt Arkiv*, **67**, 89–102.

Chicago Conference: Standardization in Human Cytogenetics (1966). *Birth Defects: Original Article Series*, II, 2. The National Foundation—March of Dimes, New York.

Ford, C. E. and Clegg, H. (1969). Reciprocal translocations. *British Medical Bulletin*, **25**, 110–114.

Giannelli, F. (1965). Autoradiographic identification of the D (13–15) chromosome responsible for D_1 trisomic Patau's syndrome. *Nature*, **208**, 669–672.

Hauschteck, E., Mürset, G., Prader, A., and Bühler, E. (1966). Siblings with different types of chromosomal aberrations due to D/E-translocation of the mother. *Humangenetik*, **5**, 281–293.

Jacobsen, P., Dupont, A., and Mikkelsen, M. (1963). Translocation in the 13–15 group as a cause of partial trisomy and spontaneous abortion in the same family. *Lancet*, **2**, 584–585.

Miller, D. A., Allerdice, P. W., Miller, O. J., and Breg, W. R. (1971). Quinacrine fluorescence patterns of human D group chromosomes. *Nature*, **232**, 24–27.

Miller, J. R., Dill, F. J., Corey, M. J., and Rigg, J. M. (1970). A rare translocation (47,XY,t(2p−;21q+),21+) associated with Down's syndrome. *Journal of Medical Genetics*, **7**, 389–393.

Murken, J. D., Bauchinger, M., Palitzsch, D., Pfeifer, H., Suschke, J., and Haendle, H. (1970). Trisomie D_2 bei einem $2\frac{1}{2}$ jährigen Mädchen (47,XX,14+). *Humangenetik*, **10**, 254–268.

Patau, K., Smith, D., Therman, E., Inhorn, S., and Wagner, H. P. (1960). Multiple congenital anomaly caused by an extra autosome. *Lancet*, **1**, 790–793.

Taylor, A. (1968). Autosomal trisomy syndromes: a detailed study of 27 cases of Edwards' syndrome and 27 cases of Patau's syndrome. *Journal of Medical Genetics*, **5**, 227–252.

Taylor, M. B., Juberg, R. C., Jones, B., and Johnson, W. A. (1970). Chromosomal variability in the D_1 trisomy syndrome. *American Journal of Diseases of Children*, **120**, 374–381.

Normal Male Development with Y Chromosome Long Arm Deletion (Yq−)*

Many observers have reported the variability in Y chromosome length and the apparent lack of any phenotypic effect attributable to a very long Y.

Short Y chromosomes have been found in normal fertile males (Borgaonkar *et al*, 1969) as well as in families with diminished fertility (Muldal and Ockey, 1962). Large deletions of the Y resulting in a fragment-like chromosome have been described in an intersex raised as a female (Lo and Kobernick, 1965), in a Turner's syndrome patient where it occurred with 45,X mosaicism (Ferguson-Smith *et al*, 1969), and in a severely retarded male baby (Nakagome *et al*, 1965). The case presented here is apparently the first in which an extreme deletion of the Y chromosome was found to be associated with fertility as well as normal male development.

Case Report

Chromosome studies were done on a 36-year-old mentally-retarded male (IQ 51), with several minor physical anomalies. He is 179 cm tall, with a normal male habitus, including heavy beard and normal external genitalia. During childhood, he had surgery for bilateral inguinal hernia and undescended testicles, but his testicles are now of normal adult size. He usually speaks with a peculiar high-pitched voice, but is capable of using deep voice tones on occasion. His chest shows pseudo-gynaecomastia, no true breast tissue being present.

The shape of the head is remarkably round, with a bilateral frontal-temporal depression and a low anterior hairline. The eyes appear deeply set, and he wears glasses for severe myopia. Brushfield spots are noted in the iris periphery. There is anteversion of both auricles, and the chin is prominent. Acne extends from his shoulders to the upper portions of his chest and back. In addition, he has numerous small, bright-red cavernous haemangiomas on the neck, arms, and scalp. Examination of the extremities shows hypoplasia of the 5th metacarpals, resulting in short-appearing 5th fingers. The big toes are short and slightly clubbed, and all of the finger and toenails are strikingly short in length.

The patient, the youngest of 4 children, was born when his mother was 32 years old. His sisters, now aged 44 and 42, have had 2 and 3 children respectively, while his 43-year-old brother has 4 children. All of his sibs and their children are normal.

Cytogenetic Studies

Chromosome studies from a peripheral blood culture showed a karyotype of 46 chromosomes, all of which appear normal with the exception of what is presumed to be the Y (Fig. 1). This is a small metacentric chromosome, less than half the size of the other G chromosomes. When stained with quinacrine, no brightly fluorescent region attributable to the Y chromosome was seen (Figs. 2 and 3). A buccal smear stained with quinacrine showed no fluorescing Y bodies.